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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,769	03/06/2006	Daniel Butzke	WEICKM-0046	5398

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,769	BUTZKE ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1 and 51-104* is/are pending in the application.

4a) Of the above claim(s) *58-63, 68-104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,51-57 and 64-67* is/are rejected.

7)☐ Claim(s) *1,51-57 and 64-67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant, on date 11/17//2006 elected with traverse Group 1 (claims 1, 51-57 and 64-67), drawn to isolated polypeptide of SEQ ID NO:2 and fragments thereof. Applicants primarily traverse the restriction between group 1 and groups 2-29 inventions by arguing that there would be no undue burden on the examiner to examine all the claims directed to L-amino acid oxidase. This is not persuasive because while the search for each of these distinct groups would be overlapping it would not be coextensive. Art that applies for amino acid oxidase, DNA, vector, transformed cells, antibodies and method of using proteins, genes, etc may or may not be relevant to the others. Therefore, groups 2-29 (claims 58-63, 68-104 of election/restriction-office action of date 10/17/2006 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Acknowledgement is made of applicant's PCT priority date based on application filing date of 01/20/2004 of PCT/EP04/00423 and foreign applications European patent office, EPO 03001232.2 filed on date 01/20/2003, European patent office, EPO 03026613.4 filed on date 11/19/2003.

Objections

Claims 1, 51-57 and 64-67 must be restricted to elected subject matter only.

Claim Rejections

35 U.S.C 112 Rejection

USC 112 2nd Paragraph rejection:

> The following is a quotation of the second paragraph of 35 U.S.C. 112: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 54-55, 64-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claim 54 is indefinite and broad in the recitation of "addition or removal of an L-amino acid" as the specification does not define from where "addition or removal of an L-amino acid" is to occurrs, ie a protein or a reaction. Claim 55 is indefinite and broad in the recitation of " derivative or a precursor of L-lysine,--" What " derivatives or a precursors of L-lysine,--" are encompassed? Claim 64 is indefinite and broad in the recitation of "optionally". The term "optionally" is vague and indefinite. Claims 65-66 are indefinite and broad in the recitation of " modulating substance" because it is unclear what is the " modulating substance" or its characteristics and how it modulates the cytotoxic activity.

35 U.S.C 112 1ST paragraph Rejections

Written Description requirement Rejections:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 56-57 and 64-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polypeptide molecules comprising either SEQ ID NO:2 or fragments thereof or any polypeptide which is at least 70% sequence identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising the said polypeptides. The specification does not contain any disclosure of the function of all the polypeptides. The genus of polypeptides that comprise these above amino acid sequences is a large variable genus comprising many different proteins. Therefore, many functionally unrelated proteins are encompassed within the scope of these claims, including partial amino acid sequences. The specification discloses only a few species of **L-amino acid oxidase from *Aplysia punctata*** of the claimed genus (SEQ ID NOs: 2, 4, 6), which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 65-67 are directed to a pharmaceutical composition or kit comprising any modulating substance that modulates cytotoxic activity of any variant of SEQ ID NO:2. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of substances or it describe how any substance can modulate any polypeptide. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Enablement Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,.51-57 and 64-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the L-amino acid oxidase of SEQ ID NO:2, or pharmaceutical kit comprising said amino acid oxidase does not reasonably provide enablement for any polypeptide molecules

comprising any fragment of SEQ ID NO:2 or any L-amino acid oxidase which is at least 70% sequence identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising said polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and for use the invention commensurate in scope with these claims.

Claims 1, 56-57 and 64 are so broad as to encompass any polypeptide molecules comprising any fragment of SEQ ID NO:2 or any L-amino acid oxidase which is at least 70% sequence identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising the said polypeptides. Claims 51-56, 66-67 are so broad as to encompass any polypeptide comprising any fragment of SEQ ID NO: 2 or any polypeptide which is at least 70% sequence identical to the polypeptide of SEQ ID NO: 2, wherein said polypeptide has amino acid oxidase activity or pharmaceutical kits comprising the said polypeptides. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number polypeptide molecules broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this

case the disclosure is limited to the amino acid sequences of only a few amino acid oxidases (SEQ ID Nos: 2, 4 and 6).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., Whisstock, et al. Quarterly Rev. Biophy. 2003, 36, pp 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims 1, 51-57, 64-67 which encompass any protein having 70% identity to SEQ ID NO: 2 of said proteins because the specification does **not** establish the desired activity; (A) regions of the protein structure which may be modified without effecting amino acid oxidase activity; (B) the general tolerance of amino acid oxidase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid oxidase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any

polypeptide with an enormous number of modifications of amino acid residues of a protein having amino acid sequence of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of amino acid oxidase polypeptide, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 65-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibitory substances L-lysine, L-arginine that inhibit the cytotoxic activity of L-amino oxidase comprising SEQ ID NOs: 2, 4, and 6, does not reasonably provide enablement for any modulating substance that modulate any polypeptide recited in the instant claims. The specification fails to describe how any substance modulates the cytotoxic activity of said polypeptides The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of substances as discussed above. As the structure of the claimed substances are not defined in any way, one of ordinary skill in the art would not be able to make and use any such substances without undue experimentation to first find what substances in fact fall within the claimed class. Furthermore, the claimed class of compounds is likely to include many compounds, which one of ordinary skill in the art would be unable to make and use without undue experimentation, even if it was known or expected that the substance be within the scope of the claims because the

specification does **not** establish: (A) regions of the modulator structure which may be modified without effecting cytotoxic activity; (B) the general tolerance of modulation to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any modulator substance structure with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any modulating substances. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of substances having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 51-57, 64-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Isaac et al. (US pat 6372211). Isaac et al. teach a L-lysine oxidase, comprising residues 120-135 of SEQ ID NO: 2. Therefore, Isaac et al. reads on any protein comprising **any fragment** of SEQ IDNO: 2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed M. Y. Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

Recombinant Enzymes, 3C31 Remsen Bld

400 Dulany Street, Alexandria, VA 22314

Telephone: 517-272-1261

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER